



SEQUENCE LISTING

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<120> CRYSTAL STRUCTURE OF BETA SITE APP CLEAVING ENZYME
(BACE) AND METHODS OF USE THEREOF

<130> 674553-2002.1

<140> 10/627,473

<141> 2003-07-25

<150> 60/398,681

<151> 2002-07-26

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<170> PatentIn Ver. 2.1

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Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
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Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His
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Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala
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Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu
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Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu
 65          70          75          80

Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
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Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His
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Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu
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 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys
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 Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu
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 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
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Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
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Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala
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Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	245	250	255
Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	260	265	270
Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	275	280	285
Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	290	295	300
Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	305	310	315
Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	325	330	335

Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu
 340 345 350
 Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu
 355 360 365
 Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe
 370 375 380
 Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met
 385 390 395 400
 Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe
 405 410 415
 Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val
 420 425 430
 Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile
 435 440 445
 Pro Gln Thr Asp Glu Ser
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<210> 11
 <211> 1386
 <212> DNA
 <213> Homo sapiens

<400> 11
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 ctggggctgc ggctgccccg ggagaccgac gaagagcccc aggagcccc caagaagggc 180
 agctttgttg agatggtgga caacctgagg ggcaagtcgg ggcagggcta ctacgtggag 240
 atgaccgtgg gcagccccc gcagacgctc aacatcctgg tggatacagg cagcagtaac 300
 tttgcagtgg gtgctgcccc ccaccccttc ctgcatcgct actaccagag gcagctgtcc 360
 agcacatacc gggacctccg gaagggtgtg tatgtgccct acaccaggg caagtgggaa 420
 ggggagctgg gcaccgacct ggtaagcatc ccccatggcc cccaggtcac tgtgcgtgcc 480
 aacattgctg ccatcactga atcagacaag ttcttcatcc agggctccaa ctgggaaggc 540
 atcctggggc tggcctatgc tgagattgcc aggcctgacg actccctgga gcctttcttt 600
 gactctctgg taaagcagac ccacgttccc aacctcttct ccctgcagct ttgtggtgct 660
 ggcttcccc tccagcagtc tgaagtgtg gcctctgtcg gagggagcat gatcattgga 720
 ggtatcgacc actcgctgta cacaggcagt ctctggtata caccatccg gcgggagtg 780
 tattatgagg tgatcattgt gcgggtggag atcaatggac aggatctgaa aatggactgc 840
 aaggagtaca actatgacaa gagcattgtg gacagtggca ccaccaacct tcgtttgcc 900
 aagaaagtgt ttgaagctgc agtcaaattc atcaaggcag cctcctccac ggagaagttc 960
 cctgatggtt tctggctagg agagcagctg gtgtgctggc aagcaggcac cacccttgg 1020
 aacattttcc cagtcatttc actctaccta atgggtgagg ttaccagca gtccttccgc 1080
 atcaccatcc ttccgcagca atacctgcgg ccagtggaa atgtggccac gtcccaagac 1140
 gactgttaca agtttgccat ctacagtc tccacgggca ctgttatggg agctgttatc 1200
 atggagggct tctacgttgt ctttgatcgg gccgaaaac gaattggctt tgctgtcagc 1260
 gcttgccatg tgacagatga gttcaggacg gcagcgggtg aaggcccttt tgtcacctg 1320
 gacatggaag actgtggcta caacattcca cagacagatg agtcacatca ccatcatcac 1380
 cactaa 1386

<210> 12
 <211> 461
 <212> PRT
 <213> Homo sapiens

<400> 12

Met	Ala	Ser	Met	Thr	Gly	Gly	Gln	Gln	Met	Gly	Arg	Gly	Ser	Met	Ala
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Gly	Val	Leu	Pro	Ala	His	Gly	Thr	Gln	His	Gly	Ile	Arg	Leu	Pro	Leu
			20					25					30		
Arg	Ser	Gly	Leu	Gly	Gly	Ala	Pro	Leu	Gly	Leu	Arg	Leu	Pro	Arg	Glu
		35					40					45			
Thr	Asp	Glu	Glu	Pro	Glu	Glu	Pro	Gly	Lys	Lys	Gly	Ser	Phe	Val	Glu
	50					55					60				
Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu
65					70					75					80
Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr
				85					90					95	
Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His
			100					105						110	
Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys
		115					120					125			
Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly
	130					135					140				
Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Gln	Val	Thr	Val	Arg	Ala
145					150					155					160
Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Gln	Gly	Ser
				165					170					175	
Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro
		180						185					190		
Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His
		195					200					205			
Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu
	210					215					220				
Gln	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly
225					230					235					240
Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile
				245					250					255	
Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn
			260					265					270		

Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser
 275 280 285
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe
 290 295 300
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe
 305 310 315 320
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly
 325 330 335
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly
 340 345 350
 Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr
 355 360 365
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys
 370 375 380
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile
 385 390 395 400
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
 405 410 415
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala
 420 425 430
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn
 435 440 445
 Ile Pro Gln Thr Asp Glu Ser His His His His His His
 450 455 460

<210> 13
 <211> 1368
 <212> DNA
 <213> Homo sapiens

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 ctggggctgc ggctgccccg ggagaccgac gaagagcccg aggagcccg caagaagggc 180
 agctttgtgg agatggtgga caacctgagg ggcaagtgcg ggcagggcta ctacgtggag 240
 atgaccgtgg gcagccccc gcagacgctc aacatcctgg tggatacagg cagcagtaac 300
 ttgacagtgg gtgctgcccc ccaccccttc ctgcatcgct actaccagag gcagctgtcc 360
 agcacatacc gggacctccg gaagggtgtg tatgtgccct acaccaggga caagtgggaa 420
 ggggagctgg gcaccgacct ggtaagcatc ccccatggcc cccaggtcac tgtgcgtgcc 480
 aacattgctg ccatcactga atcagacaag ttcttcatcc agggctccaa ctgggaaggc 540
 atcctggggc tggcctatgc tgagattgcc aggcctgacg actccctgga gcctttcttt 600
 gactctctgg taaagcagac ccacgttccc aacctcttct ccctgcagct ttgtggtgct 660
 ggcttcccc tccagcagtc tgaagtgtcg gcctctgtcg gagggagcat gatcattgga 720
 ggtatcgacc actcgctgta cacaggcagt ctctgtgata caccatccg gcgggagtg 780
 tattatgagg tgatcattgt gcgggtggag atcaatggac aggatctgaa aatggactgc 840

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aaggagtaca actatgacaa gagcattgtg gacagtggca ccaccaacct tcgtttgccc 900
aagaaagtgt ttgaagctgc agtcaaattcc atcaaggcag cctcctccac ggagaagttc 960
cctgatgggtt tctggctagg agagcagctg gtgtgctggc aagcaggcac cacccttgg 1020
aacattttcc cagtcatttc actctaccta atgggtgagg ttaccagca gtccttccgc 1080
atcaccatcc ttccgcagca atacctgcgg ccagtggagg atgtggccac gtccaagac 1140
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gcttgccatg tgcacgatga gttcaggacg gcagcggtgg aaggcccttt tgtcaccttg 1320
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<210> 14

<211> 455

<212> PRT

<213> Homo sapiens

<400> 14

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Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly Arg Gly Ser Met Ala
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Gly Val Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu
      20              25              30

Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu
      35              40              45

Thr Asp Glu Glu Pro Glu Glu Pro Gly Lys Lys Gly Ser Phe Val Glu
  50              55              60

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu
  65              70              75              80

Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
      85              90              95

Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His
      100             105             110

Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys
      115             120             125

Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly
      130             135             140

Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val Thr Val Arg Ala
      145             150             155             160

Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Gln Gly Ser
      165             170             175

Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro
      180             185             190

Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His
      195             200             205

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Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu
 210 215 220
 Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly
 225 230 235 240
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile
 245 250 255
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn
 260 265 270
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser
 275 280 285
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe
 290 295 300
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe
 305 310 315 320
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly
 325 330 335
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly
 340 345 350
 Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr
 355 360 365
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys
 370 375 380
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile
 385 390 395 400
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
 405 410 415
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala
 420 425 430
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn
 435 440 445
 Ile Pro Gln Thr Asp Glu Ser
 450 455

<210> 15

<211> 1386

<212> DNA

<213> Homo sapiens

<400> 15

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 gccacggca cccagcacgg catccggctg cccctgcgca gcggcctggg gggcgcccc 120


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ctggggctgc ggctgccccg ggagaccgac gaagagcccg aggagcccg cgggaagggc 180
agctttgtgg agatggtgga caacctgagg ggcaagtcgg ggcagggcta ctacgtggag 240
atgaccgtgg gcagcccccc gcagacgctc aacatcctgg tggatacagg cagcagtaac 300
tttgagtggt gtgctgcccc ccaccccttc ctgcatcgct actaccagag gcagctgtcc 360
agcacatacc gggacctccg gaagggtgtg tatgtgccct acaccaggg caagtgggaa 420
ggggagctgg gcaccgacct ggtaagcatc ccccatggcc ccaggtcac tgtgcgtgcc 480
aacattgctg ccatcactga atcagacaag ttcttcatcc agggctccaa ctgggaaggc 540
atcctggggc tggcctatgc tgagattgcc aggcctgacg actccctgga gcctttcttt 600
gactctctgg taaagcagac ccacgttccc aacctcttct ccctgcagct ttgtggtgct 660
ggcttcccc tccagcagtc tgaagtgtg gcctctgtcg gagggagcat gatcattgga 720
ggatcgacc actcgctgta cacaggcagt ctctggtata caccatccg gcgggagtgg 780
tattatgagg tgatcattgt gcgggtggag atcaatggac aggatctgaa aatggactgc 840
aaggagtaca actatgacaa gagcattgtg gacagtggca ccaccaacct tcgtttgccc 900
aagaaagtgt ttgaagctgc agtcaaatcc atcaaggcag cctcctccac ggagaagttc 960
cctgatgggt tctggctagg agagcagctg gtgtgtgctg aagcaggcac cacccttgg 1020
aacattttcc cagtcattct actctaccta atgggtgagg ttaccagca gtccttccgc 1080
atcacatcc ttccgcagca atacctgcgg ccagtggaa atgtggccac gtcccaagac 1140
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atggagggct tctacgttgt ctttgatcgg gcccgaatac gaattggctt tgctgtcagc 1260
gcttgccatg tgcacgatga gttcaggacg gcagcggtgg aaggcccttt tgtcaccttg 1320
gacatggaag actgtggcta caacattcca cagacagatg agtcacatca ccatcatcac 1380
cactaa 1386

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<210> 16

<211> 461

<212> PRT

<213> Homo sapiens

<400> 16

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Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly Arg Gly Ser Met Ala
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Gly Val Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu
      20                      25                      30

Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu
      35                      40                      45

Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Lys Gly Ser Phe Val Glu
      50                      55                      60

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu
      65                      70                      75                      80

Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
      85                      90                      95

Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His
      100                      105                      110

Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys
      115                      120                      125

Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly
      130                      135                      140

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Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val Thr Val Arg Ala
 145 150 155 160
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Gln Gly Ser
 165 170 175
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro
 180 185 190
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His
 195 200 205
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu
 210 215 220
 Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly
 225 230 235 240
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile
 245 250 255
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn
 260 265 270
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser
 275 280 285
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe
 290 295 300
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe
 305 310 315 320
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly
 325 330 335
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly
 340 345 350
 Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr
 355 360 365
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys
 370 375 380
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile
 385 390 395 400
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
 405 410 415
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala
 420 425 430
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn
 435 440 445

Ile Pro Gln Thr Asp Glu Ser His His His His His His
 450 455 460

<210> 17
 <211> 1383
 <212> DNA
 <213> Homo sapiens

<400> 17
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 ctggggctgc ggctgccccg ggagaccgac gaagagcccg aggagcccg caggggcagc 180
 tttgtggaga tgggtggacaa cctgaggggc aagtcggggc agggctacta cgtggagatg 240
 accgtgggca gccccccgca gacgctcaac atcctgggtg atacaggcag cagtaacttt 300
 gcagtgggtg ctgcccccca ccccttctct catcgctact accagaggca gctgtccagc 360
 acataccggg acctccggaa ggggtgtgtat gtgccctaca cccagggcaa gtgggaaggg 420
 gagctgggca ccgacctggg aagcatcccc catggccccc aggtcactgt gcgtgccaac 480
 attgctgcca tcaactgaatc agacaagttc ttcattccagg gctccaactg ggaaggcatc 540
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 ttccccctcc agcagtctga agtgctggcc tctgtcggag ggagcatgat cattggaggt 720
 atcgaccact cgctgtacac aggcagtctc tgggtatacac ccatccggcg ggagtggat 780
 tatgaggtga tcattgtgcg ggtggagatc aatggacagg atctgaaaat ggactgcaag 840
 gagtacaact atgacaagag cattgtggac agtggcacca ccaaccttcg tttgccaag 900
 aaagtgtttg aagctgcagt caaatccatc aaggcagcct cctccacgga gaagtccct 960
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 taa 1383

<210> 18
 <211> 460
 <212> PRT
 <213> Homo sapiens

<400> 18
 Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly Arg Gly Ser Met Ala
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 Gly Val Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu
 20 25 30
 Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu
 35 40 45
 Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Gly Ser Phe Val Glu Met
 50 55 60
 Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met
 65 70 75 80

Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly
 85 90 95
 Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg
 100 105 110
 Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly
 115 120 125
 Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr
 130 135 140
 Asp Leu Val Ser Ile Pro His Gly Pro Gln Val Thr Val Arg Ala Asn
 145 150 155 160
 Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Gln Gly Ser Asn
 165 170 175
 Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp
 180 185 190
 Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val
 195 200 205
 Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Gln
 210 215 220
 Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly
 225 230 235 240
 Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg
 245 250 255
 Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly
 260 265 270
 Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile
 275 280 285
 Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu
 290 295 300
 Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro
 305 310 315 320
 Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr
 325 330 335
 Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu
 340 345 350
 Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu
 355 360 365
 Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe
 370 375 380

Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met
385 390 395 400

Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe
405 410 415

Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val
420 425 430

Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile
435 440 445

Pro Gln Thr Asp Glu Ser His His His His His His
450 455 460

<210> 19

<211> 411

<212> PRT

<213> Homo sapiens

<400> 19

Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Lys Lys Gly
1 5 10 15

Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly
20 25 30

Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile
35 40 45

Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His
50 55 60

Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg
65 70 75 80

Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu
85 90 95

Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val
100 105 110

Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe
115 120 125

Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu
130 135 140

Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val
145 150 155 160

Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala
165 170 175

Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser
180 185 190

Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp
 195 200 205
 Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg
 210 215 220
 Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn
 225 230 235 240
 Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro
 245 250 255
 Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser
 260 265 270
 Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys
 275 280 285
 Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu
 290 295 300
 Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu
 305 310 315 320
 Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp
 325 330 335
 Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met
 340 345 350
 Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg
 355 360 365
 Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe
 370 375 380
 Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp
 385 390 395 400
 Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser
 405 410

<210> 20

<211> 411

<212> PRT

<213> Homo sapiens

<400> 20

Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Lys Lys Gly
 1 5 10 15

Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly
 20 25 30

Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile
 35 40 45
 Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His
 50 55 60
 Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg
 65 70 75 80
 Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu
 85 90 95
 Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val
 100 105 110
 Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe
 115 120 125
 Ile Gln Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu
 130 135 140
 Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val
 145 150 155 160
 Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala
 165 170 175
 Gly Phe Pro Leu Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser
 180 185 190
 Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp
 195 200 205
 Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg
 210 215 220
 Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn
 225 230 235 240
 Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro
 245 250 255
 Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser
 260 265 270
 Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys
 275 280 285
 Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu
 290 295 300
 Tyr Leu Met Gly Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu
 305 310 315 320
 Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp
 325 330 335

Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met
 340 345 350
 Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg
 355 360 365
 Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe
 370 375 380
 Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp
 385 390 395 400
 Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser
 405 410

 <210> 21
 <211> 417
 <212> PRT
 <213> Homo sapiens

 <400> 21
 Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Lys Lys Gly
 1 5 10 15
 Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly
 20 25 30
 Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile
 35 40 45
 Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His
 50 55 60
 Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg
 65 70 75 80
 Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu
 85 90 95
 Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val
 100 105 110
 Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe
 115 120 125
 Ile Gln Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu
 130 135 140
 Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val
 145 150 155 160
 Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala
 165 170 175
 Gly Phe Pro Leu Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser
 180 185 190

Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp
195 200 205

Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg
210 215 220

Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn
225 230 235 240

Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro
245 250 255

Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser
260 265 270

Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys
275 280 285

Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu
290 295 300

Tyr Leu Met Gly Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu
305 310 315 320

Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp
325 330 335

Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met
340 345 350

Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg
355 360 365

Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe
370 375 380

Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp
385 390 395 400

Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser His His His His His
405 410 415

His

<210> 22

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 22

agctccctct cctgagaagc cacc

<210> 23
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 23
 ccacaggtgc catctgtgtc tcc 23

<210> 24
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 24
 caccagcacc acccagactt gg 22

<210> 25
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 25
 aaccacggag gtgtggtcca gg 22

<210> 26
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 26
 cccgaggagc ccggcaagaa gggcagcttt gtggagatg 39

<210> 27
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 27
 catctccaca aagctgccct tcttgccggg ctctcggg 39

<210> 28

<211> 40
 <212> DNA
 <213> Homo sapiens

<400> 28
 cccgaggagc ccggccggaa gggcagcttt gtggagatgg 40

<210> 29
 <211> 40
 <212> DNA
 <213> Homo sapiens

<400> 29
 ccatctccac aaagctgccc ttccggccgg gctcctcggg 40

<210> 30
 <211> 42
 <212> DNA
 <213> Homo sapiens

<400> 30
 cccgaggagc ccggcagggg cagctttgtg gagatggtgg ac 42

<210> 31
 <211> 42
 <212> DNA
 <213> Homo sapiens

<400> 31
 gtccaccatc tccacaaagc tgcccctgcc gggctcctcg gg 42

<210> 32
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 32
 cccgaggagc ccggcaagaa gggcagcttt gtggagatg 39

<210> 33
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 33
 catctccaca aagctgccct tcttgccggg ctctcggg 39

<210> 34
 <211> 40
 <212> DNA
 <213> Homo sapiens

<400> 34
 cccgaggagc ccggccggaa gggcagcttt gtggagatgg 40

<210> 35
 <211> 40
 <212> DNA
 <213> Homo sapiens

<400> 35
 ccatctccac aaagctgccc ttccggccgg gctcctcggg 40

<210> 36
 <211> 42
 <212> DNA
 <213> Homo sapiens

<400> 36
 cccgaggagc ccggcagggg cagctttgtg gagatgggtgg ac 42

<210> 37
 <211> 42
 <212> DNA
 <213> Homo sapiens

<400> 37
 gtccaccatc tccacaaagc tgcccctgcc gggctcctcg gg 42

<210> 38
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 38
 cccgaggagc ccggcaagaa gggcagcttt gtggagatg 39

<210> 39
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 39
 catctccaca aagctgccct tcttgccggg ctctcggg 39

<210> 40
 <211> 40
 <212> DNA
 <213> Homo sapiens

<400> 40
 ccacagacag atgagtcatg acaccatcat caccactaag 40

<210> 41
 <211> 40
 <212> DNA
 <213> Homo sapiens

<400> 41
 cttagtgggtg atgatgggtgt catgactcat ctgtctgtgg

40

<210> 42
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: 6-His tag

<400> 42
 His His His His His His
 1 5

<210> 43
 <211> 29
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 43
 cgggatccat ggcgggagtg ctgcctgcc

29

<210> 44
 <211> 40
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 44
 cgggatcctt atgactcatc tgtctgtgga atgttgtagc

40

<210> 45
 <211> 18
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: His tag
 oligonucleotide sequence

<400> 45
catcaccatc atcaccac

18

<210> 46
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Illustrative
synthetic flourescent peptide

<400> 46
Arg Glu Glu Val Asn Leu Asp Ala Glu Phe Lys Arg
1 5 10